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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,385	11/12/2001	Carol W. Readhead	20040351.DIB	3519

23595 7590 06/17/2008

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EXAMINER	
HAMA, JOANNE	
ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
06/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/008,385	READHEAD ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *135,137,138,140-143 and 145-160* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *135,137,138,140-143 and 145-160* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/22/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

In view of the Appeal Brief filed on December 4, 2006, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Peter Paras, Jr/

Supervisory Patent Examiner, Art Unit 1632

DETAILED ACTION

The status of the claims, filed September 16, 2005, is as follows. Claims 1-134, 136, 139, 144 are cancelled.

Claims 135, 137, 138, 140-143, 145-160 are under consideration.

Withdrawn Rejection

35 USC § 103

Applicant's arguments, see pages 7-23 of Applicant's Appeal Brief, filed December 4, 2006, with respect to the rejection of claims 135, 137, 138, 140-143, 145-160 as being obvious over Brinster and Zimmerman, 1994, in view of Vogel and Sarver, 1995 have been fully considered. The Examiner withdraws the rejection because the 102 rejection, described below, anticipates the claimed invention. The rejection of claims 135, 137, 138, 140-143, 145-160 has been withdrawn.

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 135, 137, 138, 140, 142, 143, 145-160 are newly rejected under 35 U.S.C. 102(e) as being anticipated by Brinster et al., US Patent 5,858,354, patented January 12, 1999, previously cited, as evidenced by Cotten et al., 1995, Virology, 213-494-502.

The claims are directed to in vitro methods of incorporating at least one polynucleotide encoding a desired trait into a male germ cell comprising obtaining a male germ cell from a non-human vertebrate, transfecting the germ cell in vitro with at least one polynucleotide encoding a gene product and allowing the polynucleotide to be taken up and released into the germ cell.

Brinster et al. teach a method of in vitro transfection primitive cells, such as spermatogonial stem cells (Brinster et al., col. 5-7, especially, col. 5, line 66) with a heterologous DNA sequence encoding a gene of interest (Brinster et al., col. 8, lines 33-49). Brinster et al. teach that the heterologous DNA sequence can be transferred into the primitive cells by a viral vector, such as a retroviral vector or an adenoviral vector, or by liposomes (Brinster et al., col., 7, line 66 to col. 8, line 9). Brinster et al. further teach that the DNA sequence may be obtained from a source of the same species as the primitive cells, but this is not absolutely required (Brinster et al., col. 8, lines 50-55). Brinster et al. teach that the heterologous DNA sequences are operatively linked to promoters or enhancers (Brinster et al., column 8, lines 56-59). Brinster et al. further teach that such methods may be applicable to any species of animals including human, in which the male has testes (Brinster et al., col. 10, lines 27-43). Brinster et al. further

teach that sperm comprising the transgene construct can be tracked by including a nucleic acid sequence encoding a genetic marker (e.g. lacZ) operably linked to a sperm-specific promoter (here, Zfy-1, which is active in developing sperm cells) (Brinster et al., col., 11, line 58 to col. 12, line 19). Brinster et al. also teach that after introduction of the transgene construct to sperm, the sperm can be introduced to the seminiferous tubules of a host male animal (Brinster et al., col., 13, lines 14-17). Brinster et al. teach that progeny mice comprising the transgene were obtained following treatment of sperm with a transgene (Brinster et al., col., 18, lines 57-60, col., 19, lines 4-6).

With regard to the claims being drawn to the temperature of the transfection (claim 138), Brinster et al. teach that male germ cells are cultured at 32°C because of their sensitivity to high temperatures (Brinster et al., col. 6, lines 30-32). While Brinster et al. teach the temperature used for culturing, as far as can be told, the temperature used for culturing would be the same as that used for transfection.

With regard to the claims being drawn to use of an adenoviral vector having endosomal lytic activity (claim 142), it is inferred that the adenoviral vector which Brinster et al. teach that can be used to introduce into sperm (Brinster et al., col. 8, line 31) has lytic activity. Cotten et al. teach that lysis of the endosome is required before the virus enters the host cell.

With regard to the claims being drawn to specifically named promoter used to drive expression of the genetic selection marker (claim 146), while Brinster et al. do not specifically teach any of the promoters listed in claim 146, Brinster et al. do teach that

sperm-specific promoters (which c-kit, c-raf, and DAZ) are envisioned to be used in their method. As such, using any promoter that expresses specifically in sperm is design choice.

With regard to the cells being inject via the vasa efferentia (claim 157), while Brinster et al. teach injection of sperm directly into the testis, injection of the sperm through the vasa efferntia, the duct that connects the rete testis to the epididymis, is a matter of design choice.

With regard to the claim being drawn to using the method to correct a gene disorder (claim 160), Brinster et al. teach that their method has applications in gene therapy, wherein the expression system is used to deliver a functional gene whose RNA or protein product will produce the desired biochemical effect in the target cell or tissue (Brinster et al., col., 2, lines 18-31). Brinster et al. teach that their method can be used to express a gene of interest including those that stimulate the immune system (Brinster et al., col., 8, lines 33-49).

Thus, the teachings of Brinster et al. anticipate the claimed invention.

It is noted that this rejection was of record October 6, 2003, page 7. While the Examiner had withdrawn the rejection July 26, 2005, upon further consideration, the Examiner reinstates the rejection as Brinster et al. anticipates the claims. It is noted that while the Office Action, July 26, 2005, page 4 had been withdrawn because Brinster et al. do not teach integration of a viral vector in the sperm genome, it is noted that Brinster et al. teach that the claimed invention can be practiced with viruses that

integrate into the genome, including those of retroviral and adenoviral vectors. As such, the rejection of Brinster et al. is reinstated.

In response to Applicant's rebuttals, filed August 30, 2004, pages 10-11, wherein Applicant indicates that Brinster et al., US Patent 5,858,354, does not anticipate the claimed invention, Applicant indicates that there is no disclosure in Brinster that it is male germ cells that are modified genetically. Brinster et al. disclose primitive cells including totipotent cells and embryonic stem cells, but do not specify which of these are to be modified (Applicant's response, page 10). In response, Brinster et al. envisioned that all types of primitive cells can be used in the claimed invention (Brinster et al., col. 4, lines 30-37). Claim 135 includes that "spermatogonial stem cells" be one of the types of cells that are treated with a viral expression vector. Because Brinster et al. teach "primitive" germ cells, Brinster et al. anticipate the claimed invention. In addition to this, it is noted that Brinster et al. also teach that a mixture of male gonadal cells obtained from donor testes was introduced into recipient mice. Brinster et al. teach that mice between postnatal days 21-28 provided quiescent Sertoli cells and germ cell distribution approaching that of mature testes (Brinster et al., col. 16, lines 38-40) and that donor cells comprising a transgene established normal spermatogenesis in Busulfan-treated recipients (Brinster et al., col. 17, lines 47-50). As such, Brinster et al. teach different types of male gonadal cells can be used to practice the claimed invention.

Applicant indicates that the teaching of Brinster et al. would lead the skilled person away from the present invention, as Brinster et al. teach that teratocarcinoma and embryonic stem cells and not male germ cells are to be used. In response, Brinster

et al. indicates that primitive cells such as teratocarcinoma and embryonic stem cells be used because these cells have the potential to differentiate into any cell types including spermatogonial stem cells (Brinster et al., col., 4, lines 30-37). As such, this is not a teaching away from the instant invention. It is also noted that Brinster et al. teach that transgenic sperm was obtained using their method (Brinster et al., Example B) and as such, Brinster et al. provide guidance to practice the claimed invention. Applicant also indicates to emphasize the point that Brinster et al. teach away from the claimed invention was the fact that Brinster et al. used a Zfy1 promoter (Brinster et al., col. 12) is in the context of introducing a transgene into eggs to produce transgenic mice to provide the eventual donor cell. Thus, Brinster et al. do not disclose the introduction of a polynucleotide into a germ cell (Applicant's response, page 11). In response, Brinster et al. teach that the Zfy1 promoter is a sperm-specific promoter (Brinster et al., col. 12, lines 2-3) and that it can be used to drive expression of a transgene in sperm. The promoter has nothing to do with transduction into eggs. With regard to Applicant indicating that Brinster et al. teach away from the claimed invention, it is noted that Brinster et al. was applied as a 102 because Brinster et al. anticipate the claimed invention. As such, indicating that Brinster et al. "teaches away" from the claimed invention is irrelevant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 135, 140, 141 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Brinster et al., US Patent 5,858,354, in view of Naldini et al., 1996, Science, 272: 263-267, see IDS filed May 20, 2004.

As discussed above, Brinster et al. provide guidance to introduce a gene of interest to a sperm cell using a viral expression vector. While Brinster et al. teach that a wide variety of viral vectors can be used (Brinster et al., col. 8, lines 19-32), they do not specifically teach lentiviral vectors.

At the time of filing, Naldini et al. teach that lentiviral vectors can be used to deliver at transgene of interest (see entire article).

Given that Brinster et al. provide guidance that a wide variety of viral vectors can be used for delivery of a gene of interest, using another vector, i.e., a lentiviral vector, is a matter of design choice and an artisan would have been as likely to use a lentiviral vector as any other viral vector in a method of introducing a transgene to a sperm cell.

Thus, the claims are obvious.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-

272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Joanne Hama/
Art Unit 1632